

10 30 50 70
 gaattccggcgagtgaggcgctgacagggaactcggggggacatcttgacagagacccctggaccagccgccaatcgagcctccag
 90 110 130 150 170
 cccagtcctctctcgccgttctctcgcctatggaggcgccgacccgclccgggcttcgagcagcgagccggcgaggct
 190 210 230 250
 gaccccatgtggcgagagcccgtcctggaggcgagctgcgclcccccgggtcccgccccagcgccggcgcggt
 270 290 310 330
 cagcatgattcctgggttcattcttgctcctgttggcgtggctcaatcactgttggcgaacatgctactacagtttcacc
 350 370 390 410
 M D S W F I L V L F G S G L I H V S A N N A I T V S P
 430 450 470 490
 ttcttloggaacgacgaagatttaattaaacatcaacacagaattggctaaaggaggaataaacatcaacatctctc
 S L G T T R L I K T S T T E L A K E E N K T S N S T S S
 510 530 550 570 590
 agtaatttctctctgtggcaccacattcagcccaacatgactctggagccacactgtgactactgttaattcttcaca
 V I S L S V A P T F S P N L T L E P T Y V T T V N S S H
 610 630 650 670
 ctctgacaatgggacagggggcgccgacgggaatctggggacactaccatttccccgaacgggaagctggcttattggagaa
 S D N G T R R A A S T E S G G T T I S P N G S W L I E N
 690 710 730 750
 ccogttcacggatgccataacgaacccctggggggaactccagcactgcagcaaccacatccagaaacatccccccggcaga
 Q F T D A I T E P W E G N S S T A A T T P E T F P P A D
 770 790 810 830
 tgagacacccaattattcggtgatgggtggccctgctctctgtgtaactgtgttattatcatagttctgtacatgttgaag
 E T P I I A V M V A L S S L L V I V F I I I V L Y M L R
 850
 gtttaaggaatccagcaagctgggggtcatttcccaactcttccgctgtcaaatggcgacggaggatgtggagcccaag
 F K K Y K Q A G S H S N S F R L S N G R T E D V E P Q S

FIG.1A

FIG. 1C

2290 ocaagagtcggcaaatccggcagttccacttccacggctggcctggagtgaggatccccagcagcggcaaggcagatgatcaacat
 K S R Q I R Q F H F H G W P E V G I P S D C K G M I N I 2330 2350
 2370 catcgagcagtcgagaagcagcagcagcagtcggggaaccatcccatcactgacactgcagtcgagtcgcccgggagcagcagcagcagga
 I A A V Q Q Q Q Q Q S G N H P I T V H C S A G A G R T G 2410 2430 2450
 2470 oacttcgtgccttgagcacagtcctggaaacgtgtgaagcagaaggaatttttagatgtcttccaaactgtcaagagcctgcggc
 T F C A L S T V L E R V K A E G I L D V F Q T V K S L R L 2510 2530
 2550 tgcagaggccacacatggtcagacactggaaacgtgtgaattctgtctacaaggctgtacagggaatcacattgacgccttttcaga
 Q R P H M V Q T L E Q Y E F C Y J K V V Q E Y I D A F S D 2590 2610
 2630 ttatgccaaacttcaagtgacaggtgacaaggccacagacagcagcaggaattgcctttaatattttgttaattctgtttttgttgaat
 Y A N F K - 2650 2670 2690
 2710 ataccacaaattgtatatacttataactgtttttagaattggccacataggccttctattaccctgttagatggagattttgtatgta
 2730 2750 2770 2790
 2810 aatgtgttagcactgatagtccttttccagtgtttttattgggaatttaattagtgatatttgggttgatataatgaattc 2830 2850 2870

FIG.1D

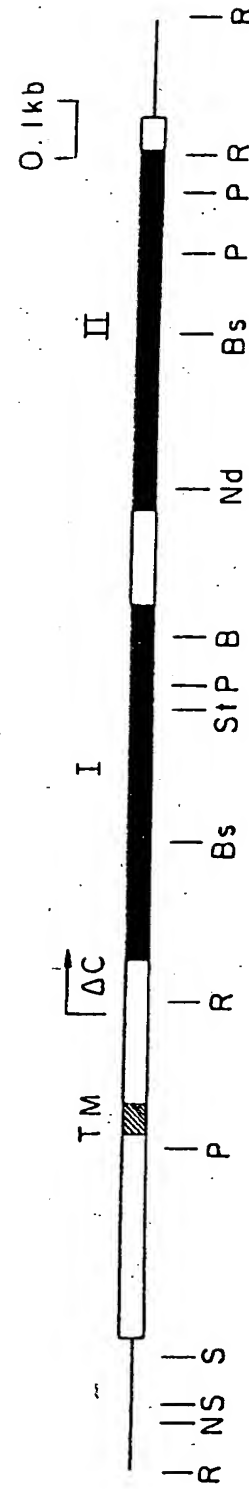


FIG.1E

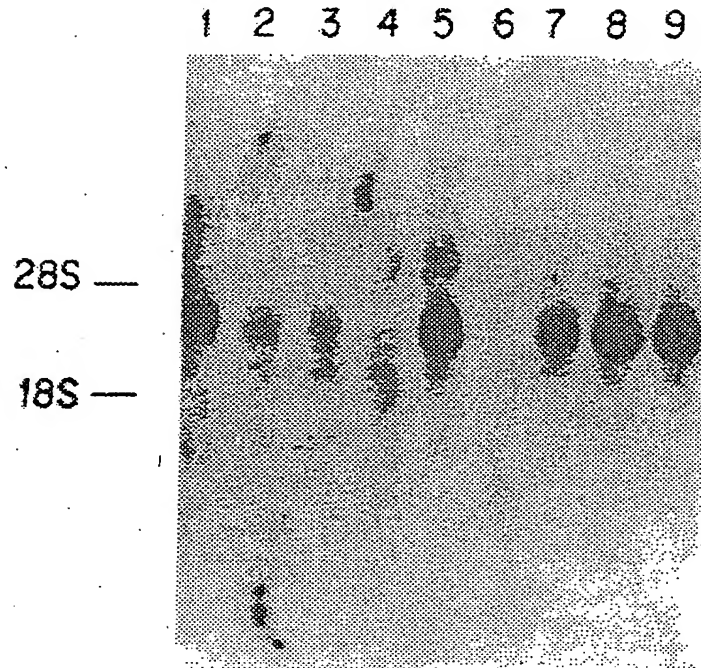


FIG. 2

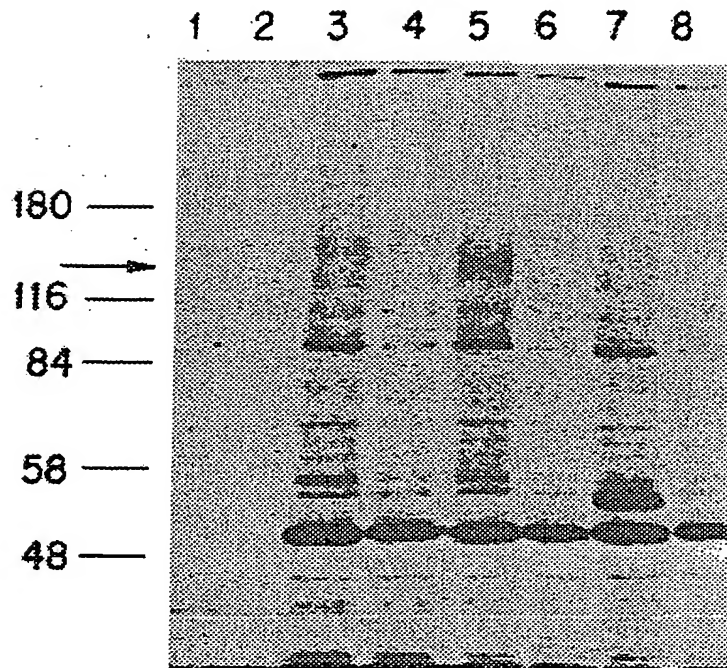


FIG. 3

FIG. 4B

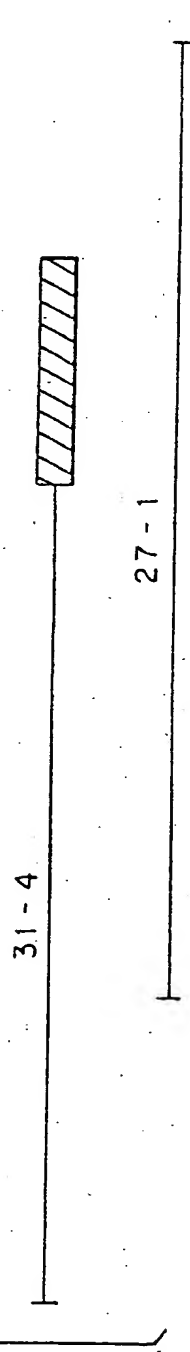
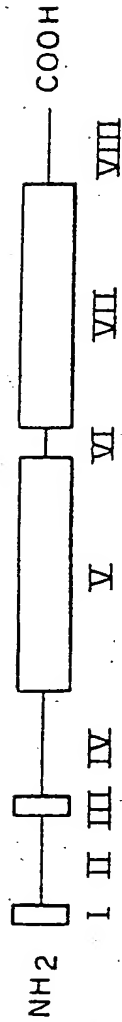


FIG. 4C



①
1 MDSWF ILVLLGSLICVS ANNAITVAPSVG ITRLINSSTAEPVKEEAKTSNPTSSLTSLSVAPTFS
2 F H S L T K T T L A N S V I
1 NITLGP TYL TTVNSSDSNGTTRTASTNSIGITISPNGTWLPDNQFTDARTEPWEGNSSTAATTPETFP
2 L E V H R A E G T S I E I
1 PSGNSDSKORRDE TPIIAVMVALSSLLVIVFIIIVLYMIRFKKYKQAGSHSNFRLSNGRTEDVEPQS
2 A
1 VPLLARSPSTNRKYPPLPVDKLEEEINRRMADDNKLFREEFNALPACP IQATCEAASKEENKEKNRYV
2
1 NILPYDHSRVHLTPVEGVPDSYINASFINGYQEKNFIAAQPKKEETVNDFWRM IWEQNTATIVMVT
2 (V)
1 NLKERKECKAQYMPDQGCWTYGNI RVSVEDTVLVDTYVRKFCIQQVQDMTNRKPQRLITQFHFTSW
2 V S V
1 PDFGVPFTPIGMLKFLKKVKACNPQYAGAIWHCSAGVGRGTGTFWIDAMLDMMHTERKVDVYGFVSR
2 S
1 IRAQRQMVQTDMQYVF IYQALLEHYLYGDTLEVTSLETHLQKIYNKIPGTSNNGLEEEFKLTSIK
2
1 IQNDKMRITGNLPANMKKNRVLIIPYEFNRVIIPVKRGEENTDYVNASFIDGYRQKDSYIASQGPLLH
2 (VII)
1 TIEDFWRM IWEWKSCSIVMLTELEERGQEKCAQYWP SDGLVSYGDI TVELKKEEECESYTVRDLLVTN
2
1 TRENKSRQIRQFHFGWPEVGIPSDGKGMISIIAAVQKQQQSGNHPITVHCSAGAGRTGTCALSTV
2 N
1 LERVKAEGILDVFQTVKSLRQRPMMVQTL EQYFCYKVVOEYIDAFSDYANFK
2

FIG. 4D

	10	20	30	40	
LCA	NqnKNRYVdILPYDynRVeL	sEinGdagSnYINASyldGfkEprKyIAA			
RPTase α	NKeKNRYVNILPYDHSRVhLtpvE	GvpdSDYINASfInGYqEknKfIAA			
RPTase β	NKHKNRYINIVAYDHSRVKLaaLaekDgKltDYINANYVDGYNrpKAYIAA				
RPTase γ	NKHKNRYINIIAYDHSRVKLrpLpgKDsKhsDYINANYVDGYNkaKAYIAA				
CON	NkhKNRY-nII-YDhsRVKL—l—k—k—sdYINA—y—dGynepk—ylAa				
	50	60	70	80	90
LCA	QGPrdETVdDFWRMIWEQkatvIVMTrceEgnrnKCAeYWPsmEegTra				
RPTase α	QGPkeETVnDFWRMIWEQntatIVMTNLkerkeckCAQYWPdqGewTYG				
RPTase β	QGPKSTaEDFWRMiWEhNvevIVMITNLVEKGRRKCDQYWPdGSEEEYG				
RPTase γ	QGPKSTfEDFWRMiWEqNtgiIVMITNLVEKGRRKCDQYWPtenSEEEYG				
CON	QGPIk-TveDFWRMIWEqnt-vIVM-TnlvEkgrRK-qYWP—gse-yg				
	100	110	120	130	
LCA	fgdVvVkinqhkrpcDYiiqKI	nIvn	kkekatgRevThiq		
RPTase α	NirVsVedVtVLv	DYTVRKFc	IqqvGd	mtnRkpqRIiTQfH	
RPTase β	NfIVTqKSVqVLA	yYTVRnFtIRNTKIKK	Gs	qKGRpsgRVVTQYH	
RPTase γ	NiIVTIKStkihAc	YTVRrFsiRNTKvKK	GqkgnpKGRqneRVViQYH		
CON	ni-Vlvk-v-vla—dYtvrkf—rntki—k—g—k—kgr—qRvvtqyh				

FIG.5A

	140	150	160	170	180	190
LCA	FTSWPDhGVPedPhlILKlrrrVnAfsnffsGpIVVHCSAGVGRTGTyigID					
RPTase α	FTSWPDfGVPfLPigmLKfIkKVkAcnpqyaGaIVVHCSAGVGRTGTfvVID					
RPTase β	YTQWPDmGVPEYsLPVLTfVRKaayAkrhavGPVVHCSAGVGRTGTyIVID					
RPTase γ	YTQWPDmGVPEYaLPVLTfVRrssaArmpetGPVIVHCSAGVGRTGTyIViD					
CON	-T-WPDmGVPeypIplvL-fvr-v-aa-Gp-vVHCSAGVGRTGTyiviD					

	200	210	220	230
LCA	AMLegleaeEnKVDVYGyVvkIRrQRCIMVQveaQYiIhQALvE			
RPTase α	AMLdmhEtErKVDVYGFVsrIRaQRCqMVQTdmQYVFlyQALIE			
RPTase β	SMLQQIqhEgTVNi fGFLKHIRsQRNYLVQTEEQYVF IHDtLvE			
RPTase γ	SMLQQIkdksTVNvIGFLKHIRtQRNYLVQTEEQYi f IHDaLIE			
CON	-MLqqi-e-V-vyGf-khIR-QR-y-VQteeQY-fIh-aL-E			

FIG.5B

	10	20	30	40
LCA	NksKNRnsnvIPYdyNRVp khe emskesehdssdessdddsdsEEpskY			
RPTase α	NmkKNRv q IPYEfNRV ipvkr			GEEnTDY
RPTase β	NrEKNRtSSIIPvERsRVG ssLs			GE GTDY
RPTase γ	NkEKNRnSSvvPsERaRVG apLp			GmkGTDY
CON	NkeKNRnss-iPyernRVg—			geegldY
	50	60	70	80
LCA	iNASF msYwkpevm AdCGPLkeT gDFWqM fqrKvkviVMLTELkhg			
RPTase α	vNASF dGYrQkdsy AsCGPLLHT eDFWRM WewKscs VMLTELeer			
RPTase β	iNASY MGYYQSNEF TQHPLLHT KDFWRM WDHNAQ VMI PDgQnm			
RPTase γ	iNASY MGYYrSNEF TQHPLpHT KDFWRM WDHNAQ iVMI PDnQs			
CON	iNAS—lmgYyqsnef —tQ—PL htikDFWRM wdh—naqiVMI—q—			
	100	110	120	130
LCA	dQEiCAQYW geGkqtYGD eVdLKdtdksstYT Rvfe rhskrkdsRrtv			
RPTase α	gQEiCAQYWPsdG lvsYGD tVeLKkeeeCESYTV Rd lvntntreNkSRq			
RPTase β	A EDEFVYWPn kDEpi NCESFkVTLmaeehkCLSNEEk l			
RPTase γ	A EDEFVYWPs reEsm NCEaFtVTLiskdr CLSNEEq l			
CON	aE—e—qYWps—g—ygd—v—lk—nces—lvt—e—r—clsne—r—i			
	150	160	170	180
LCA	yQy qY tnWsvEqIP aepKellSm qvVkQK pQk			
RPTase α	rQf HF hgWPevgiP SdgKgm SilaaV Qk Qq			
RPTase β	IQDFILEATQDDYVLEVRHFQCPKWPNPDsP SkTFEL SVI			K
RPTase γ	IhDFILEATQDDYVLEVRHFQCPKWPNPDaP SsTFEL nVI			K
CON	iqdfileatqddyvlevrhfqcpkwpnpd—Pis—t—ellsvl—			qk

FIG.5C

	190	200	210	220	230
LCA	nsseGNkhhkstP	IIiHCrdGsqq	TGiFCALIn	ILEsaetEevv	DiFQvVKa
RPTase α	qqsgNh	PitVHCsaGagr	TGTFCALsTv	LErvkaEgi	IDVFQtVKs
RPTase β	EEAaNR	DGPmIVHDEhGgVt	AGTFCALTTLmh	QLEkENsVDV	yQVAKM
RPTase γ	EEAItR	DGPtIVHDEyGaVs	AGmICALTTLsq	QLEnENaVDV	fQVAKM
CON	-eea-nr-	dgP-i vH-e-Gav-	Gt fCALt t t l l e q l e-	En-vDv fQv-Km	

	240	250
LCA	LrkaRPgMVstfEQYqFIYdVias	
RPTase α	LaLqRPhMVqTIEQYefcYKVvqe	
RPTase β	INLMRPGVFdIEQYQFIYKVILS	
RPTase γ	INLMRPGVFtIEQYQFIYKvILS	
CON	-nlmRPg-	iEQYqFIYkvils

FIG.5D

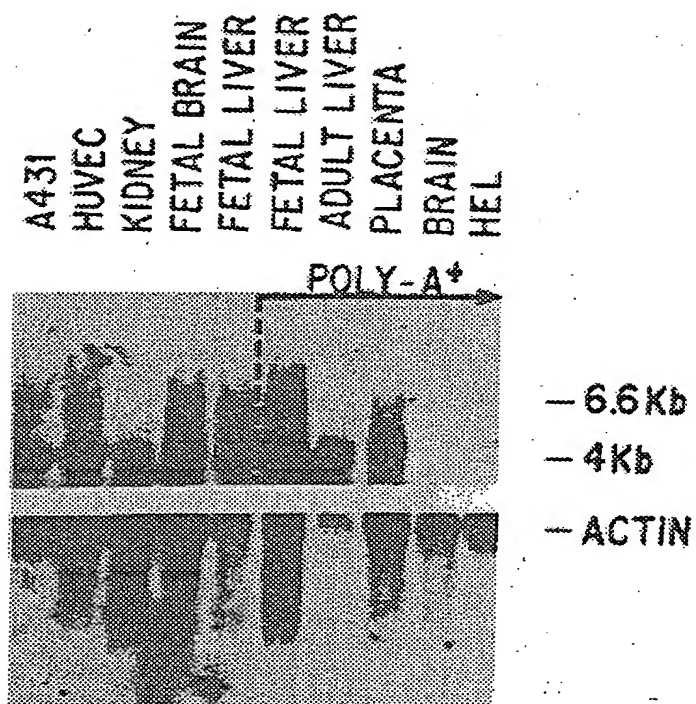
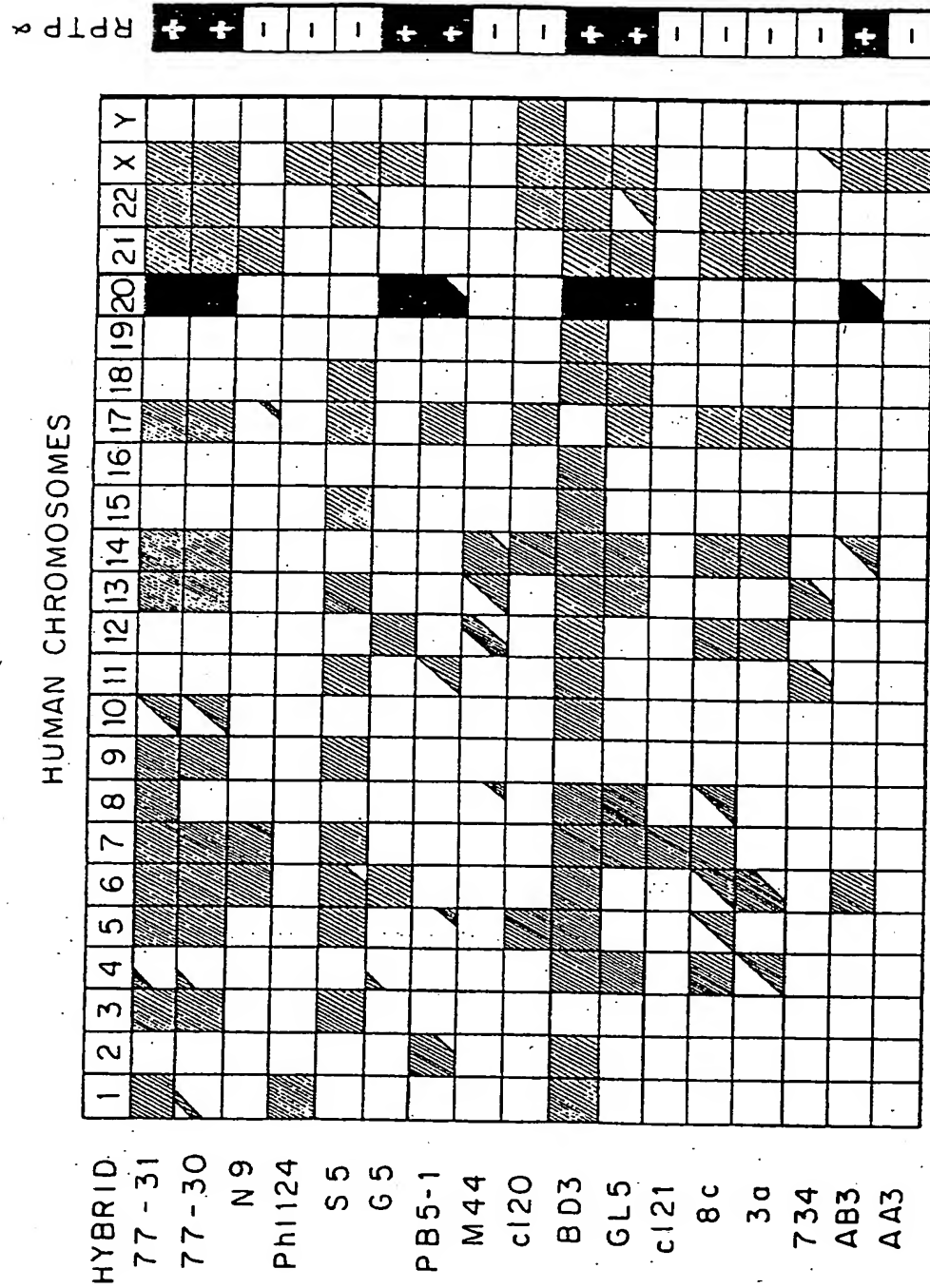


FIG. 6

FIG. 7



1 ATGGATTCTGGTTCATTCTTGTCTGCTCGGCAGTGGTCTGATATGTGTCAGTGCCAAC 60
1 [M D S W F I L V L L G S G L I C V S] A N 20
SIGNAL PEPTIDE

61 AATGCTACCACAGTTGCACCTTCTGTAGGAATTACAAGATTAACTCATCAACGGCA 120
21 N A T T V A P S V G I T R L I N S S T A 40

121 GAACCAGTTAAAGAAGAGGCCAAAACCTTCAAATCCAACTTCTTCACTAACTTCTTTTCT 180
41 E P V K E E A K T S N P T S S L T S L S 60

181 GTGCCACCAACATTCAGCCCAAATATAACTCTGGGACCCACCTATTTAACCCTGTCAAT 240
61 V A P T F S P N I T L G P T Y L T T V N 80

241 TCTTCAGACTCTGACAATGGGACCACAAGAACAGCAAGCACCAATTCTATAGGCATTACA 300
81 S S D S D N G T T R T A S T N S I G I T 100

301 ATTTACCAAATGGAACGTGGCTTCCAGATAACCAGTTCACGGATGCCAGAACAGAACCC 360
101 I S P N G T W L P D N Q F T D A R T E P 120

361 TGGGAGGGGAATTCCAGCACCGCAGCAACCACTCCAGAACTTTCCCTCCTTCAGGTAAT 420
121 W E G N S S T A A T T P E T F P P S G N 140

421 TCTGACTCGAAGGACAGAAGAGATGAGACACCAATTATTGCGGTGATGGTGGCCCTGTCC 480
141 S D S K D R R D E T [P I I A V M V A L S 160
TRANSMEMBRANE SEGMENT

481 TCTCTGCTAGTGATCGTGTTTATTATCATAGTTTGTACATGTTAAGGTTTAAGAAATAC 540
161 S L L V I V F I I I V L Y M L] R F K K Y 180

541 AAGCAAGCTGGGAGCCATTCCAATTCTTTCCGCTTATCCAACGGCCGCACTGAGGATGTG 600
181 K Q A G S H S N S F R L S N G R T E D V 200

601 GAGCCCCAGAGTGTGCCACTTCTGGCCAGATCCCCAAGCACCAACAGGAAATACCCACCC 660
201 E P Q S V P L L A R S P S T N R K Y P P 220

661 CTGCCCCGTGGACAAGCTGGAAGAGGAAATTAACCGGAGAATGGCAGACGACAATAAGCTC 720
221 L P V D K L E E E I N R R M A D D N K L 240

721 TTCAGGGAGGAATTCAACGCTCTCCCTGCATGTCCTATCCAGGCCACCTGTGAGGCTGCT 780
241 F R E E F N A L P A C P I Q A T C E A A 260

781 TCCAAGGAGGAAAAACAAGGAAAAAATCGATATGTAAACATCTTGCCTTATGACCACTCT 840
261 S K E E [N K E K N R Y V N I L P Y D H S 280
PTPase DOMAIN I

FIG.8A

841 AGAGTCCACCTGACACCGGTTGAAGGGGTTCCAGATTCTGATTACATCAATGCTTCATTC 900
281 R V H L T P V E G V P D S D Y I N A S F 300

901 ATCAACGGTTACCAAGAAAAGAACAAATTCATTGCTGCCACAAGGACCAAAAAGAAGAAACC 960
301 I N G Y Q E K N K F I A A Q G P K E E T 320

961 GTGAATGATTTCTGGCGGATGATCTGGGAACAAAACACAGCCACCATCGTCATGGTTACC 1020
321 V N D F W R M I W E Q N T A T I V M V T 340

1021 AACCTGAAGGAGAGAAAGGAGTGCAAGTGGCCCCAGTACTGGCCAGACCAAGGCTGCTGG 1080
341 N L K E R K E C K C A Q Y W P D Q G C W 360

1081 ACCTATGGGAATATTCGGGTGTCTGTAGAGGATGTGACTGTCTCTGGTGGACTACACAGTA 1140
361 T Y G N I R V S V E D V T V L V D Y T V 380

1141 CGGAAGTTCTGCATCCAGCAGGTGGGCGACATGACCAACAGAAAGCCACAGCGCCTCATC 1200
381 R K F C I Q Q V G D M T N R K P Q R L I 400

1201 ACTCAGTTCCACTTTACCAGCTGGCCAGACTTTGGGGTGCCTTTTACCCCGATCGGCATG 1260
401 T Q F H F T S W P D F G V P F T P I G M 420

1261 CTCAAGTTCCTCAAGAAGGTGAAGGCCTGTAACCCTCAGTATGCAGGGGCCATCGTGGTC 1320
421 L K F L K K V K A C N P Q Y A G A I V V 440

1321 CACTGCAGTGCAGGTGTAGGGCGTACAGGTACCTTTGTGTCATTGATGCCATGCTGGAC 1380
441 H C S A G V G R T G T F V V I D A M L D 460

1381 ATGATGCATACAGAACGGAAGGTGGACGTGTATGGCTTTGTGAGCCGGATCCGGGCACAG 1440
461 M M H T E R K V D V Y G F V S R I R A Q 480

1441 CGCTGCCAGATGGTGCAAACCGATATGCAGTATGTCTTCATATACCAAGCCCTTCTGGAG 1500
481 R C Q M V Q T D M Q Y V F I Y Q A L L E] 500

1501 CATTATCTCTATGGAGATACAGAACTGGAAGTGACCTCTCTAGAAACCCACCTGCAGAAA 1560
501 H Y L Y G D T E L E V T S L E T H L Q K 520

1561 ATTTACAACAAAATCCCAGGGACCAGCAACAATGGATTAGAGGAGGAGTTTAAGAAGTTA 1620
521 I Y N K I P G T S N N G L E E E F K K L 540

FIG.8B

1621 ACATCAATCAAAATCCAGAATGACAAGATGCGGACTGGAAACCTTCCAGCCAACATGAAG 1680
541 T S I K I Q N D K M R T G N L P A [N M K 560
PTPase Domain II
1681 AAGAACCGTGTTTTACAGATCATTCCATATGAATTCAACAGAGTGATCATTCCAGTTAAG 1740
561 K N R V L Q I I P Y E F N R V I I P V K 580
1741 CGGGGCGAAGAGAATACAGACTATGTGAACGCATCCTTTATTGATGGCTACCGGCAGAAG 1800
581 R G E E N T D Y V N A S F I D G Y R Q K 600
1801 GACTCCTATATCGCCAGCCAGGGCCCTCTTCTCCACACAATTGAGGACTTCTGGCGAATG 1860
601 D S Y I A S Q G P L L H T I E D F W R M 620
1861 ATCTGGGAGTGGAATCCTGCTCTATCGTGATGCTAACAGAACTGGAGGAGAGAGGCCAG 1920
621 I W E W K S C S I V M L T E L E E R G Q 640
1921 GAGAAGTGTGCCAGTACTGGCCATCTGATGGACTGGTGTCTATGGAGATATTACAGTG 1980
641 E K C A Q Y W P S D G L V S Y G D I T V 660
1981 GAACTGAAGAAGGAGGAGGAATGTGAGAGCTACACCGTCCGAGACCTCCTGGTCACCAAC 2040
661 E L K K E E E C E S Y T V R D L L V T N 680
2041 ACCAGGGAGAATAAGAGCCGGCAGATCCGGCAGTTCCACTTCCATGGCTGGCCTGAAGTG 2100
681 T R E N K S R Q I R Q F H F H G W P E V 700
2101 GGCATCCCCAGTGACGGAAAGGGCATGATCAGCATCATCGCCGCCGTGCAGAAGCAGCAG 2160
701 G I P S D G K G M I S I I A A V Q K Q Q 720
2161 CAGCAGTCAGGGAACCAACCCCATCACCGTGCAGTGCAGCGCCGGGGCAGGAAGGACGGGG 2220
721 Q Q S G N H P I T V H C S A G A G R T G 740
2221 ACCTTCTGTGCCCTGAGCACCGTCCTGGAGCGTGTGAAAGCAGAGGGGATTTTGGATGTC 2280
741 T F C A L S T V L E R V K A E G I L D V 760
2281 TTCCAGACTGTCAAGAGCCTGCGGCTACAGAGGCCACACATGGTCCAGACACTGGAACAG 2340
761 F Q T V K S L R L Q R P H M V Q T L E Q 780
2341 TATGAGTTCTGCTACAAGGTGGTGCAGGAGTATATTGATGCATTCTCAGATTATGCCAAC 2400
781 Y E F C Y K V V Q E] Y I D A F S D Y A N 800
2401 TTCAAGTAA 2409
801 F K * 803

FIG.8C